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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/12/2003 11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/046,924	CASES ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *3-6 and 11-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 7-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-23 are still at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-3, 7 and 8-10 and applicants election of the species of SEQ ID NO: 3, in Paper No. 10 is acknowledged. It was noted to applicants representative, Paula Borden, that the previous restriction requirement did not include an election of species corresponding to the listed sequence identifiers (i.e. SEQ ID NOs) but rather this was a requirement for restriction between these SEQ ID NOs. Applicants representative acknowledged this mistake and said that applicants election remained that of Group I, claims 1-3, 7 and 8-10 and SEQ ID NO: 3.

Applicants traverse the restriction requirement on the basis that according to the MPEP 803, if search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions. Applicants position that it would not be unduly burdensome to perform a search on claims 1-23 together is acknowledged, however applicants argument is not found persuasive because while the searches for the each of the groups overlap, they are not coextensive. For example, search of Group II would require search of subclass 530/350, a search of Group III would require search of subclass 530/387.1, search of Group IV would require search of subclass 530/350, a search of Group III would require search of subclass 530/387.1, a search of Group IV would require search of subclass 435/69.1, a search of Group V would require

search of subclass 514/789, and a search of Groups VI and VII each would require search of subclass 435/15. A search of each of these subclasses would be unnecessary the search of the elected group I. Further applicants are reminded that as pointed out by themselves, that the MPEP 803 states that if search and examination of an entire application can be made without serious burden, the examiner must examine it even on the merits. Applicants attention is drawn to the recited phrase "if search and examination of an entire application..." As discussed above, and pointed out to applicants that even the "search" of the different groups is burdensome given the of different groups of inventions for the reasons previously stated. Further the additional examination, in addition to the search, of the different Groups adds even more burden to the search and examination, then merely the search as discussed above.

Claims 3, 4-6 and 11-23 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

Applicants statement on the first line of the specification to state that this application is a continuation-in-part of U.S. Patent Application Serial No. 09/794,715, filed February 26, 2001, which application claims priority to the filing date of the U.S. Provisional Application Serial No. 60/271,307, filed February 23, 2001, the disclosures of which are herein incorporated by reference is acknowledged.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosure, Paper No. 3, filed 4/26/2002 and Paper No. 4, filed 12/9/2002, is acknowledged. Those references considered have been initialed.

Specification

The disclosure is objected to because of the following informalities: Applicants list a number of amino and nucleic acid sequences in the figures, most of which are also accompanied by a sequence identifier (i.e. SEQ ID NO), with the following exceptions: Figure 8A lists four sequences, the fourth of which has no associated SEQ ID NO either in the figure or in the description of the figure. Figure 10A shows a comparison of two amino acid sequences with no associated SEQ ID NOs.

> **2422.02** The Requirement for Exclusive Conformance; Sequences Presented in Drawing Figures
> ... It should be noted, though, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the seque identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings.

Appropriate correction is required.

Claim Objections

Claims 1-3 and 7-10 are objected to because of the following informalities:

Claim 2 recites "DGAT2α" . It is suggested that in the first claim in which DGAT2α is to be used applicants spell out the recited abbreviation in full, followed by (DGAT2α).

In claim 7, line 1, after "transcriptional initiation region" it is suggested that applicants place a comma in order to present a clearer claim.

In claim 7, line 2, it is suggested that applicants change "nucleic acid according to Claim 1", to "polynucleotide according to Claim 1", to maintain consistency throughout the claims and present a clearer claim.

Claims 1-3 and 7-10 contain non-elected subject matter.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite in the recitation of "DGAT2α" as the specification fails to teach which identifying characteristics distinguish a "DGAT2α" from other proteins

having diacylglycerol transferase enzymatic activity. The application teaches characteristics of the disclosed polynucleotides (nucleic acid sequence of DGAT2α polynucleotides from both mouse and human, etc.) but fails to define what is necessary for inclusion of a polynucleotide which is distinct in sequence from SEQ ID NO: 1 or 3, to be considered to be within this class.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2 and 7-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide comprising a nucleic acid sequence of SEQ ID NO: 3, wherein said polynucleotide encodes a polypeptide with DGAT activity, does not reasonably provide enablement for any polynucleotide which encodes a polypeptide that exhibits diacylglycerol transferase activity wherein said polynucleotide has a mere 50% identity to SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1, 2 and 7-10 are so broad as to encompass any polynucleotide encoding a polypeptide which exhibits diacylglycerol transferase activity, wherein said polynucleotide comprises a nucleotide sequence at least 50% identical to SEQ ID NO: 3 (claims 1 and 2), an expression cassette (vector) and host cells comprising said polynucleotide (claims 7-9) and a method of expressing said polynucleotide (claim 10). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims, including all polynucleotides which encode any mammalian diacylglycerol transferase having a mere 50% sequence identity to SEQ ID NO: 3. Since the amino acid sequence of a protein determines its structural and functional properties and the amino acid sequence of a protein is determined by the encoding nucleic acid sequence, predictability of which changes can be tolerated in a protein's or its encoding polynucleotide sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to that polynucleotide comprising SEQ ID NO: 3, wherein said polynucleotide encodes a polypeptide with diacylglycerol transferase activity.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's or polynucleotide's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide which encodes a polypeptide with diacylglycerol transferase activity, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting diacylglycerol transferase activity; (B) the general tolerance of diacylglycerol transferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a diacylglycerol transferase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the diacylglycerol transferase activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem

and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus having diacylglycerol transferase activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polynucleotide having a mere 50% sequence identity to SEQ ID NO: 3 and encoding a polypeptide with diacylglycerol transferase activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 7-10 are rejected under 35 U.S.C. 102(a) as being anticipated by Baker et al. (WO 00/12708, March 2000, See IDS ref).

Baker et al. teach a number of human polynucleotides which encode membrane-bound proteins including that polynucleotide shown in Figure 163, which encodes the transmembrane protein pro1433 shown in Figure 164. The polynucleotide taught by Baker et al. is greater than 89% identical over the entire length of instantly disclosed SEQ ID NO: 3. Baker et al. further teach vectors and host cells comprising said polynucleotide, and methods of producing the encoded polypeptide by expression of said polynucleotide. While Baker et al. does not teach that the disclosed polynucleotide encodes a "DGAT2α polypeptide", this is considered to be an inherent property of the polynucleotide taught by Baker et al. based on the extremely high sequence identity to instantly disclosed SEQ ID NO: 3 and SEQ ID NO: 1.

Thus Baker et al. anticipates claim 1 drawn to a polynucleotide encoding a polypeptide which exhibits diacylglycerol transferase activity wherein said polynucleotide has at least 50% identity to SEQ ID NO: 3 (Claims 1 and 2), an expression cassette (vector) comprising a transcriptional initiation and termination region functionally linked to said polynucleotide (claim 7), a host cell comprising said expression cassette (vector) (claim 8 and 9) and a method of expressing the polypeptide encoded by said polynucleotide (claim 10).

Claims 1, 2 and 7-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Specht et al. (WO 99/47655, September 1999, See IDS ref).

Specht et al. teach human nucleic acid sequences from breast tissue coding for genetic products and the polypeptides which can be obtained from said sequences. Specht et al. specifically teach a sequence, Sequence 21, which is 90% identical from nucleotide 548 through 1167 of instantly disclosed SEQ ID NO: 3 and which is 100% identical from nucleotide 552 through 1231 of instantly disclosed SEQ ID NO: 1 Specht et al. further teach expression cassettes and host cells comprising said polynucleotide sequence and methods of expression of said polynucleotide. While Specht et al. does not teach that the disclosed polynucleotide encodes a "DGAT2α product", based on the extremely high sequence identity (100%) to instantly disclosed SEQ ID NO: 1, the polynucleotide taught by Specht et al. inherently encodes a DGAT2α polypeptide .

Thus, Specht et al. anticipate claims 1, 2 and 7-10.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned

are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
August 8, 2003